Claims:

Please amend the claims as follows, and cancel claims 52-53, 66-67, and 68-70, without prejudice:

1. **(Currently Amended)** A computer-implemented method for quantifying relative gene relatedness for a plurality of candidate genes for which a plurality of gene expression level observations have been collected, the method comprising:

for a predicted **candidate** gene selected from the **plurality of** candidate genes, selecting a plurality of ~~selected~~ subset **gene** combinations of the plurality of candidate genes, and performing (a)-(c) for each subset **gene** combination to generate a plurality of quantifications of relative relatedness for the predicted **candidate** gene and the subset combinations:

(a) based on data comprising the plurality of gene expression level observations for the plurality of candidate genes, constructing a **multivariate** nonlinear model predicting gene expression for the predicted **candidate** gene, wherein the **multivariate** nonlinear model accepts gene expression levels for the subset **gene** combination of the plurality of candidate genes as inputs and produces a gene expression level for the predicted **candidate** gene as an output;

(b) predicting gene expression of the predicted **candidate** gene with the **multivariate** nonlinear model; and

(c) measuring effectiveness of the **multivariate** nonlinear model in accurately predicting the gene expression level of the predicted **candidate** gene as compared to the gene expression level observations, the effectiveness being a quantification of relative gene relatedness of the predicted gene and the subset **gene** combination of the plurality of candidate genes with respect to other subset **gene** combinations of the **plurality of** candidate genes **as determined by comparing effectiveness of the multivariate nonlinear model with effectiveness of other multivariate nonlinear models constructed for other subset gene combinations, the other multivariate nonlinear models being of a same type as the multivariate nonlinear model**; and

presenting a ranked plurality of the plurality of quantifications of relative gene relatedness for a plurality of the subset **gene** combinations of the **plurality of** candidate genes.

2. (Original) A computer-readable medium comprising computer-readable instructions for performing the method of claim 1.

3. (Original) The method of claim 1 wherein the nonlinear model accepts a plurality of predictive elements as inputs, wherein at least one of the predictive elements indicates whether a gene expression observation is associated with having applied a particular external stimulus to biological material.

4. (Previously Presented) The method of claim 1 further comprising:

accepting by the nonlinear model a plurality of predictive elements as inputs, wherein at least one of the predictive elements indicates whether a gene expression observation is associated with a particular cell state.

5. (Previously Presented) The method of claim 1 further comprising:

accepting by the nonlinear model a plurality of predictive elements as inputs, wherein at least one of the predictive elements indicates differential gene expression between two samples of biological material.

6. (Original) The method of claim 1 wherein the nonlinear model comprises a multivariate prediction function accepting two or more inputs to predict gene expression.

7. (Canceled)

8. (Original) The method of claim 1 wherein constructing the nonlinear model predicting gene expression comprises choosing a nonlinear model from a constrained set of nonlinear models.

9. (Original) The method of claim 1 wherein measuring the model's effectiveness comprises evaluating the model to estimate a coefficient of determination for an optimal model estimated by the model.

10. (Original) The method of claim 1 wherein the nonlinear model predicting gene expression is a full-logic model predicting gene expression for a predicted candidate gene, and the effectiveness of the model is measured by comparing predictions of gene expression for the predicted candidate gene by the model with observations of gene expression for the predicted candidate gene.

11. (Previously Presented) The method of claim 1 further comprising:

obtaining the plurality of gene expression level observations from results of a plurality of cDNA microarray experiments measuring mRNA transcription levels for a plurality of genes in biological material.

12. (Original) The method of claim 1 wherein the data comprising a plurality of gene expression observations is divided into a training set of data and a test set of data, wherein

the nonlinear model predicting gene expression is generated via the training set data; and

effectiveness of the nonlinear model is measured via the test set of data.

13. (Original) The method of claim 12 wherein the training set of data is extended by randomly reordering and recycling gene expression observations.

14. (Original) The method of claim 1 wherein

a plurality of training data sets are repeatedly chosen from the data comprising a plurality of gene expression observations;

the nonlinear model is one of a plurality of models constructed from the plurality of training data sets; and

quantification of the relatedness for the plurality of candidate genes is measured by measuring average effectiveness of the plurality of models constructed from the plurality of training data sets.

15. **(Currently Amended)** The method of claim ~~1~~ 3 further comprising:

for at least one of the predictive elements, to determine contribution of ~~a~~ **the** predictive element to the quantification of relatedness, constructing an additional nonlinear model predicting gene expression, wherein the additional nonlinear model has the predictive element as a single input, and measuring the effectiveness of the additional nonlinear model.

16. (Original) The method of claim 1 wherein the nonlinear model predicting gene expression is a truth table predicting a gene expression level for a predicted candidate gene from predictive elements comprising expression level observations for candidate genes other than the predicted candidate gene.

17. (Original) The method of claim 16 wherein the truth table comprises ternary discrete values.

18. (Original) The method of claim 16 wherein gene expression levels in the truth table are ternary discrete values.

19. (Original) The method of claim 16 wherein

the truth table comprises a plurality of rows for possible combinations of expression level observations for the candidate genes other than the predicted candidate gene; and

for at least one of the rows, the truth table indicates predicted gene expression for the predicted candidate gene with a thresholded weighted average of gene expression level observations associated with the row.

20. (Original) The method of claim 1 wherein the nonlinear model predicting gene expression is a neural network predicting gene expression.

21. (Original) The method of claim 20 wherein the neural network consists of one neuron which predicts a gene expression level for a single predicted candidate gene.

22. (Original) The method of claim 21 wherein the neuron is a ternary perceptron accepting predictive elements as inputs, wherein the predictive elements comprise gene expression levels indicated as one of three possible values: up, unchanged, and down.

23. (Original) The method of claim 22 further comprising:

displaying a three-dimensional graph representing the ternary perceptron with two planes separating points on the graph into points relating to like predicted values.

24. (Original) The method of claim 22 further comprising:

displaying a three-dimensional graph representing the ternary perceptron with objects at points in three-dimensional space within the graph, wherein axes of the graph relate to thresholded gene expression levels for three of the candidate genes.

25. (Original) The method of claim 24 wherein the objects are of a color indicating a predicted gene expression level.

26. (Original) The method of claim 24 wherein the objects are of a size indicating a number of observations related to a point on the graph.

27. (Original) The method of claim 1 wherein the data comprising a plurality of gene expression observations comprises gene expression level observations generated by subjecting sample biological material to an experimental condition and observing regulation of mRNA transcription levels for a plurality of genes in the biological material as a result of being subjected to the experimental condition.

28. (Original) The method of claim 27 wherein the data comprising a plurality of gene expression observations further comprises an indication of the experimental condition to which the biological material related to an observation was subjected and the indication is included in the model to predict gene expression.

29. (Previously Presented) A computer-implemented method for identifying genes related to a target gene by analyzing gene expression level observations for the genes, the method comprising:

based on the gene expression level observations, constructing multivariate nonlinear predictors that predict an expression level for the target gene, wherein the predictors accept gene expression levels for other genes as predictive elements;

estimating a coefficient of determination for sets of predictive elements and the target gene by comparing results of the multivariate nonlinear predictors with gene expression level observations for the target gene, wherein the predictive elements comprise expression level observations for groups of genes other than the target gene; and

ranking the groups of genes other than the target gene by coefficient of determination to present the groups of genes other than the target gene in order of likelihood of relatedness to the target gene.

30. (Original) The method of claim 29 further comprising:

indicating a proper subset of the genes having the highest likelihood of relatedness to the target gene.

31. (Original) A computer-implemented method for analyzing gene expression level observations for a set of genes comprising a target gene, the method comprising:

estimating a coefficient of determination for an optimal multivariate nonlinear model predicting gene expression of the target gene by constructing a multivariate nonlinear model from the gene expression level observations of gene expression for the target gene, wherein the optimal multivariate nonlinear model and the constructed multivariate nonlinear model predict gene expression of the target gene based on variables representing gene expression levels of genes other than the target gene.

32. (Original) The method of claim 31 wherein the optimal multivariate nonlinear model and the constructed multivariate nonlinear model predict gene expression based, at least in part, on inputs comprising an indication of a condition to which biological material relating to the observations has been subjected.

33. (Previously Presented) A method for identifying related genes out of a set of genes for which gene expression level observations have been collected, the method comprising:

for at least one predicted gene out of the set of genes, training an artificial intelligence function to predict gene expression for the predicted gene, wherein the artificial intelligence function takes one or more predictive elements as inputs and produces a gene expression level for the predicted gene as an output, wherein at least one of the predictive elements is a gene expression level for a gene other than the predicted gene;

testing effectiveness of the artificial intelligence function in predicting expression of the predicted gene to rate relative relatedness of the predicted gene and at least one gene associated with the predictive elements; and

presenting the relative relatedness in a computer user interface showing a ranking of relative relatedness for a plurality of gene groups.

34. (Original) The method of claim 33 wherein the artificial intelligence function takes a plurality of predictive elements as inputs.

35. (Original) The method of claim 33 wherein the predictive elements comprise a variable indicating biological material was subjected to an experimental condition.

36. (Original) For a plurality of observed genes for which expression levels have been observed, a method of presenting an analysis of the expression levels to assist in identifying related genes, the method comprising:

denoting a particular observed gene as a predicted gene;

for the predicted gene, constructing a plurality of nonlinear multivariate models predicting expression of the observed gene, wherein the nonlinear multivariate models comprise a variety of predictive elements chosen from permutations of expression levels of observed genes other than the predicted gene;

measuring effectiveness of the nonlinear multivariate models in predicting expression of the predicted gene to quantify relatedness between the predicted gene and the set of genes associated with the predictive elements of the models; and

presenting a quantification of relatedness between the predicted gene and a set of genes associated with the predictive elements of at least one of the models.

37. (Original) The method of claim 36 further comprising:

for a set of predictive elements and a predicted gene, displaying a graph indicating the amount of increase in the effectiveness of the model for each of the predictive elements.

38. (Original) The method of claim 36 wherein at least two of the plurality of nonlinear multivariate models predicting expression of the observed gene are implemented in specialized hardware circuits for predicting gene expression.

39. (Original) The method of claim 36 further comprising:

displaying a user interface for evaluating the analysis, wherein the user interface comprises display elements graphically indicating the relatedness of the predicted gene to a plurality of gene sets.

40. (Original) The method of claim 39 further comprising:

displaying only those display elements indicating sets of genes in which each gene in the set improves the relatedness.

41. (Original) The method of claim 39 further comprising:

accepting as input a set of one or more designated predictor genes;

accepting as input a threshold relatedness;

accepting as input a set of one or more designated predicted genes; and

limiting the display elements of the user interface to those sets of genes having as members the one or more designated predictor genes and having at least the threshold relatedness for the one or more designated predicted genes.

42. (Original) The method of claim 39 further comprising:

accepting as input a set of one or more designated predictor genes; and

limiting display elements of the user interface to those sets of genes having the one or more designated predictor genes.

43. (Original) The method of claim 42 further comprising:

accepting as input a threshold increase in relatedness; and

further limiting display elements of the user interface to those sets of genes for which addition of the one or more designated predictor genes increases the relatedness by at least the threshold increase in relatedness.

44. (Original) The method of claim 36 further comprising presenting a ranking of gene sets according to their relatedness, wherein the ranking indicates which genes are in the sets.

45. (Original) The method of claim 44 wherein the ranking further indicates contribution of individual predictive elements to the effectiveness of the models.

46. (Original) The method of claim 36 wherein the predictive elements comprise a variable indicative of whether biological material related to a gene expression observation has been subjected to a particular condition.

47. (Previously Presented) For a plurality of observed genes for which expression levels have been observed, a method of performing an analysis of the expression levels to assist in identifying related genes, the method comprising:

(a) for a plurality of the observed genes, denoting a particular observed gene as a predicted gene and performing at least (b) and (c);

(b) for the predicted gene, constructing a plurality of nonlinear multivariate models predicting expression of the predicted gene, wherein the nonlinear multivariate models have a variety of predictive elements chosen from permutations of expression levels of observed genes other than the predicted gene;

(c) measuring effectiveness of the nonlinear multivariate models in predicting expression of the predicted gene to provide a quantification of relative relatedness between the predicted gene and genes associated with the predictive elements of the models.

48. (Original) The method of claim 47 further comprising:

skipping designating genes having fewer than a defined number of changes in expression level as predicted genes.

49. (Original) The method of claim 47 further comprising:

displaying a user interface comprising display elements indicating gene relatedness for a plurality of genes associated with the predictive elements for a plurality of predicted genes.

50. (Previously Presented) A system for quantifying gene relatedness for a plurality of candidate genes for which a plurality of gene expression level observations have been collected, the system comprising:

means for constructing a nonbinary, nonlinear model predicting gene expression based on data comprising the plurality of gene expression level observations for the plurality of candidate genes;

means for predicting gene expression with the nonbinary, nonlinear model; and

means for measuring effectiveness of the nonbinary, nonlinear model in predicting gene expression, the effectiveness indicating gene relatedness for the plurality of candidate genes.

51. **(Currently Amended)** The ~~method~~ **system** of claim 50 wherein the means for predicting gene expression is **selected from the group consisting of:** a specialized hardware circuit**, a decision tree, and a truth table chosen from a constrained set of truth tables**.

52. (Canceled)

53. (Canceled)

54. (Canceled)

55. (Canceled)

56. (Canceled)

57. (Canceled)

58. (Canceled)

59. (Canceled)

60. (Canceled)

61. (Previously Presented) A computer-implemented method of ranking the relatedness of a plurality of genes based on gene expression level observations associated with the plurality of genes, the method comprising:

based on the gene expression level observations, constructing a plurality of multivariate nonlinear predictors to predict the expression of a plurality of target genes out of the genes, wherein the multivariate nonlinear predictors comprise predictive elements comprising an observed gene, thereby associating the multivariate nonlinear predictor with the target gene and at least one observed gene;

testing effectiveness of the plurality of multivariate nonlinear predictors in predicting gene expression to quantify relative gene relatedness between the genes associated with the predictors by estimating a coefficient of determination; and

displaying a ranked list of relative gene relatedness among the genes as determined by testing the plurality of multivariate nonlinear predictors.

62. (Previously Presented) The method of claim 1 wherein the gene relatedness indicates relatedness within a network controlling gene expression.

63. (Previously Presented) The method of claim 1 wherein the gene relatedness indicates relatedness based on chains of interaction among various mechanisms.

64. (Previously Presented) A computer-implemented method for analyzing a plurality of candidate genes for which a plurality of gene expression level observations have been collected to determine which out of the genes are more related, the method comprising:

for a plurality of selected permutations of the plurality of candidate genes, performing (a)-(c) for each permutation:

(a) based on data comprising the plurality of gene expression level observations for the plurality of candidate genes, constructing a nonlinear model predicting gene expression for the permutation of the plurality of candidate genes;

(b) predicting gene expression with the nonlinear model; and

(c) measuring effectiveness of the nonlinear model in predicting gene expression, the effectiveness being a quantification indicating relative gene relatedness for the plurality of candidate genes of the permutation; and

presenting at least one of the permutations of genes as related and an indication of the quantification indicating relative gene relatedness for the at least one of the permutations.

65. (Previously Presented) The method of claim 64 wherein the gene relatedness indicates relatedness within a network controlling gene expression.

66. (Canceled)

67. (Canceled)

68-70. (Canceled)

71. (New) A computer-implemented method comprising:

constructing a first multivariate nonlinear model for predicting a gene expression level for a candidate gene selected out of an observed set of genes, wherein the gene expression level for the candidate gene is predicted by the first multivariate nonlinear model via observed gene expression levels for a first permutation subset of genes selected out of the observed set of genes, the first nonlinear model taking observed gene expression levels for the first permutation subset of genes as inputs;

measuring effectiveness of the first multivariate nonlinear model in predicting the observed gene expression level of the candidate gene;

constructing a second multivariate nonlinear model for predicting the gene expression level for the candidate gene selected out of the observed set of genes, wherein the gene expression level for the candidate gene is predicted by the second multivariate nonlinear model via observed gene expression levels for a second permutation subset of genes selected out of the observed set of genes, the second nonlinear model taking observed gene expression levels for the second permutation subset of genes as inputs, wherein the first multivariate nonlinear model and the second multivariate nonlinear model are of a same model type, wherein the first multivariate nonlinear model and the second multivariate nonlinear model predict the gene expression level for the candidate gene, and wherein the first multivariate nonlinear model and the second multivariate nonlinear model are constructed via gene expression data from a same set of experiments;

measuring effectiveness of the second multivariate nonlinear model in predicting the observed gene expression level of the candidate gene;

ordering the first and second multivariate nonlinear models by ranking the effectiveness of the first multivariate nonlinear model with respect to the effectiveness of the second multivariate nonlinear model; and

presenting results of the ordering, wherein the results indicate that observed gene expression levels for a permutation subset of genes associated with a higher-ranking multivariate nonlinear model have a higher effectiveness in predicting the observed gene expression level of the candidate gene than those of observed gene expression levels for a permutation subset of genes associated with a lower-ranking multivariate nonlinear model.

72. (New) The method of claim 71, wherein the higher-ranking multivariate nonlinear model having the higher effectiveness of the two models is presented as indicating a higher relatedness between the genes that comprise the permutation subset and the candidate gene of the higher-ranking multivariate nonlinear model relative to relatedness between the genes that comprise the permutation subset and the candidate gene of the lower-ranking multivariate nonlinear model.

73. (New) The method of claim 71, further comprising:

with additional permutation subsets, constructing additional multivariate nonlinear models predicting expression levels for a gene other than the candidate gene;

measuring effectiveness for the additional multivariate nonlinear models; and

including results for the additional multivariate nonlinear models in the presenting.

74. (New) The method of claim 71, wherein the model type is a neural network.

75. (New) The method of claim 71, wherein the first permutation subset of the genes is a proper subset of the second permutation subset of the genes.

76. (New) The method of claim 71, wherein measuring effectiveness of a multivariate nonlinear model comprises evaluating the multivariate nonlinear model to determine a coefficient of determination that represents ability of the model to accurately predict the gene expression level of the candidate gene.

77. (New) A computer-readable medium comprising computer-readable instructions for performing the method of claim 71.

78. (New) The computer-implemented method of claim 71, further comprising:

constructing one or more additional multivariate nonlinear models for predicting the gene expression level for the candidate gene selected out of the observed set of genes, wherein the gene expression level for the candidate gene is predicted via observed gene expression levels for additional permutation subsets of genes selected out of the observed set of genes, and wherein the first, second, and the one or more additional multivariate nonlinear models are of the same model type and constructed from same training data;

measuring effectiveness of the one or more additional multivariate nonlinear models in predicting the observed gene expression level of the candidate gene;

in the ordering, including the one or more additional multivariate nonlinear models with the first and second multivariate nonlinear models; and

in the presenting, including the one or more additional multivariate nonlinear models with the first and second multivariate nonlinear models.

79. (New) The method of claim 78, wherein the one or more additional multivariate nonlinear models predict the gene expression level of the candidate gene by further including at least one predictive element with the additional permutation subsets of genes.

80. (New) The method of claim 79, further comprising:

to determine contribution of a predictive element or individual gene to the prediction of the expression level of the candidate gene, constructing an additional nonlinear model of a same model type using a same training set, wherein the additional nonlinear model has the predictive element or individual gene as a single predictor, and measuring the effectiveness of the additional nonlinear model.

81. (New) The method of claim 79, wherein the at least one predictive element indicates whether a gene expression observation is associated with having applied a particular external stimulus to biological material.

82. (New) The method of claim 79, wherein the at least one predictive element indicates whether a gene expression observation is associated with a particular cell state.

83. (New) The method of claim 79, wherein the at least one predictive element indicates differential gene expression between two samples of biological material.

84. (New) The method of claim 71, wherein the model type is a full-logic model.

85. (New) The computer-implemented method of claim 71, wherein the genes that comprise the permutation subset in the higher-ranking multivariate nonlinear model exhibit more predictive power in predicting the observed gene expression of the candidate gene than the genes that comprise the permutation subset in the lower-ranking multivariate nonlinear model.

86. (New) The method of claim 71, wherein the observed gene expression levels for the observed set of genes are obtained from results of a plurality of cDNA microarray experiments measuring mRNA transcription levels for a plurality of genes in biological material.

87. (New) The method of claim 71 wherein data comprising a plurality of gene expression observations is divided into a training set of data and a test set of data, wherein

the first and second multivariate nonlinear models are constructed via the training set data; and

effectiveness of the first and second multivariate nonlinear models are measured via the test set of data.

88. (New) The method of claim 87, wherein the training set of data is extended by randomly reordering and recycling gene expression observations.

89. (New) The method of claim 74, wherein the neural network consists of one neuron which predicts a gene expression level for the candidate gene.

90. (New) The method of claim 89 wherein the neuron is a ternary perceptron accepting gene expression levels as input, and wherein the gene expression levels are indicated as one of three possible values: up, unchanged, and down.

91. (New) The method of claim 90 further comprising:

displaying a three-dimensional graph representing the ternary perceptron with two planes separating points on the graph into points relating to like predicted values.

92. (New) The method of claim 90 further comprising:

displaying a three-dimensional graph representing the ternary perceptron with objects at points in three-dimensional space within the graph, wherein axes of the graph relate to thresholded gene expression levels for three of the candidate genes.

93. (New) The method of claim 92 wherein the objects are of a color indicating a predicted gene expression level.

94. (New) The method of claim 92 wherein the objects are of a size indicating a number of observations related to a point on the graph.

95. (New) The method of claim 71 wherein the observed gene expression levels for the observed set of genes comprise gene expression level observations generated by subjecting sample biological material to an experimental condition and observing regulation of mRNA transcription levels for a plurality of genes in the biological material as a result of being subjected to the experimental condition.

96. (New) The method of claim 95 wherein the observed gene expression levels for the observed set of genes further comprise an indication of the experimental condition to which the biological material related to an observation was subjected and the indication is included in the first and second multivariate nonlinear models to predict gene expression of the candidate gene.